```
     (FILE 'HOME' ENTERED AT 15:01:54 ON 23 JUN 2003)

     FILE 'MEDLINE' ENTERED AT 15:02:11 ON 23 JUN 2003
L1            13 S TSG101 AND GAG
L2           957 S GAG AND TUMOR
L3             0 S L2 AND COMPLES
L4            91 S L2 AND COMPLEX
L5            20 S L4 AND INTERACTION
L6            20 S L5 NOT L1

=>
```

	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 15:02:11 ON 23 JUN 2003

FILE LAST UPDATED: 21 JUN 2003 (20030621/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s tsg101 and gag
            92 TSG101
         10319 GAG
          1334 GAGS
         10868 GAG
                (GAG OR GAGS)
L1          13 TSG101 AND GAG

=> display l1
ENTER ANSWER NUMBER OR RANGE (1):1-13
ENTER DISPLAY FORMAT (BIB):bib abs
```

L1 ANSWER 1 OF 13 MEDLINE
AN 2003244477 IN-PROCESS
DN 22652006 PubMed ID: 12767222
TI Role of Myristylation in HIV-1 **Gag** Assembly.
AU Bouamr Fadila; Scarlata Suzanne; Carter Carol
CS Departments of Molecular Genetics & Microbiology and Physiology & Biophysics, Stony Brook University, Stony Brook, New York 11794.
SO BIOCHEMISTRY, (2003 Jun 3) 42 (21) 6408-17.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030528
Last Updated on STN: 20030528
AB Assembly of the human immunodeficiency virus type 1 (HIV-1) first occurs on the plasma membrane of host cells where binding is driven by strong electrostatic interactions between the N-terminal matrix (MA) domain of the structural precursor polyprotein, **Gag**, and the membrane. MA is also myristylated, but the exact role this modification plays is not clear. In this study, we compared the protein oligomerization and membrane binding properties of Myr(+) and Myr(-) **Gag**(MA) expressed in COS-1 cells. Sedimentation studies in solution showed that both the myristylated **Gag** precursor and the mature MA product were detected in larger complexes than their unmyristylated counterparts, and the myristylated MA protein bound liposomes with approximately 3-fold greater affinity than unmyristylated MA. Aromatic residues near the N-terminal region of the MA protein were more accessible to chymotrypsin in the unmyristylated form and, consistent with this, an epitope in the N-terminal region was more exposed. Moreover, the cyclophilin binding site in the CA domain downstream of MA was more accessible in the unmyristylated **Gag** protein, while the **Tsg101** binding site in the C-terminal region was equally available in the unmyristylated and myristylated **Gag** proteins. Taken together, our results suggest that myristylation promotes assembly by inducing conformational changes and facilitating MA multimerization. This observation offers a

novel role for myristylation.

L1 ANSWER 2 OF 13 MEDLINE
AN 2003221930 MEDLINE
DN 22628510 PubMed ID: 12743307
TI Defects in human immunodeficiency virus budding and endosomal sorting induced by **TSG101** overexpression.
AU Goila-Gaur Ritu; Demirov Dimiter G; Orenstein Jan M; Ono Akira; Freed Eric O
CS Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-0460, USA.
SO JOURNAL OF VIROLOGY, (2003 Jun) 77 (11) 6507-19.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200306
ED Entered STN: 20030514
Last Updated on STN: 20030613
Entered Medline: 20030612
AB Retrovirus budding is greatly stimulated by the presence of **Gag** sequences known as late or L domains. The L domain of human immunodeficiency virus type 1 (HIV-1) maps to a highly conserved Pro-Thr-Ala-Pro (PTAP) sequence in the p6 domain of **Gag**. We and others recently observed that the p6 PTAP motif interacts with the cellular endosomal sorting protein **TSG101**. Consistent with a role for **TSG101** in virus release, we demonstrated that overexpressing the N-terminal, **Gag**-binding domain of **TSG101** (TSG-5') suppresses HIV-1 budding by blocking L domain function. To elucidate the role of **TSG101** in HIV-1 budding, we evaluated the significance of the binding between **Gag** and TSG-5' on the inhibition of HIV-1 release. We observed that a mutation in TSG-5' that disrupts the **Gag/TSG101** interaction suppresses the ability of TSG-5' to inhibit HIV-1 release. We also determined the effect of overexpressing a panel of truncated **TSG101** derivatives and full-length **TSG101** (TSG-F) on virus budding. Overexpressing TSG-F inhibits HIV-1 budding; however, the effect of TSG-F on virus release does not require **Gag** binding. Furthermore, overexpression of the C-terminal portion of **TSG101** (TSG-3') potently inhibits budding of not only HIV-1 but also murine leukemia virus. Confocal microscopy data indicate that TSG-F and TSG-3' overexpression induces an aberrant endosome phenotype; this defect is dependent upon the C-terminal, Vps-28-binding domain of **TSG101**. We propose that TSG-5' suppresses HIV-1 release by binding PTAP and blocking HIV-1 L domain function, whereas overexpressing TSG-F or TSG-3' globally inhibits virus release by disrupting the cellular endosomal sorting machinery. These results highlight the importance of **TSG101** and the endosomal sorting pathway in virus budding and suggest that inhibitors can be developed that, like TSG-5', target HIV-1 without disrupting endosomal sorting.

L1 ANSWER 3 OF 13 MEDLINE
AN 2003147815 MEDLINE
DN 22550081 PubMed ID: 12663786
TI Role of ESCRT-I in retroviral budding.
AU Martin-Serrano Juan; Zang Trinity; Bieniasz Paul D
CS Aaron Diamond AIDS Research Center and The Rockefeller University, New York, New York 10016, USA.
NC R01 AI52774 (NIAID)
SO JOURNAL OF VIROLOGY, (2003 Apr) 77 (8) 4794-804.
Journal code: 0113724. ISSN: 0022-538X.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20030331
Last Updated on STN: 20030506
Entered Medline: 20030505
AB Retroviral late-budding (L) domains are required for the efficient release of nascent virions. The three known types of L domain, designated according to essential tetrapeptide motifs (PTAP, PPXY, or YPDL), each bind distinct cellular cofactors. We and others have demonstrated that recruitment of an ESCRT-I subunit, **Tsg101**, a component of the class E vacuolar protein sorting (VPS) machinery, is required for the budding of viruses, such as human immunodeficiency virus type 1 (HIV-1) and Ebola virus, that encode a PTAP-type L domain, but subsequent events remain undefined. In this study, we demonstrate that VPS28, a second component of ESCRT-I, binds to a sequence close to the **Tsg101** C terminus and is therefore recruited to the plasma membrane by HIV-1 **Gag**. In addition, we show that **Tsg101** exhibits a multimerization activity. Using a complementation assay in which **Tsg101** is artificially recruited to sites of HIV-1 assembly, we demonstrate that the integrity of the VPS28 binding site within **Tsg101** is required for particle budding. In addition, mutation of a putative leucine zipper or residues important for **Tsg101** multimerization also impairs the ability of **Tsg101** to support HIV-1 budding. A minimal multimerizing **Tsg101** domain is a dominant negative inhibitor of PTAP-mediated HIV-1 budding but does not inhibit YPDL-type or PPXY-type L-domain function. Nevertheless, YDPL-type L-domain activity is inhibited by expression of a catalytically inactive mutant of the class E VPS ATPase VPS4. These results indicate that all three classes of retroviral L domains require a functioning class E VPS pathway in order to effect budding. However, the PTAP-type L domain appears to be unique in its requirement for an intact, or nearly intact, ESCRT-I complex.

L1 ANSWER 4 OF 13 MEDLINE
AN 2003087613 MEDLINE
DN 22487410 PubMed ID: 12598123
TI The HIV-**TSG101** interface: recent advances in a budding field.
AU Freed Eric O
CS Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-0460, USA.. EFreed@nih.gov
SO TRENDS IN MICROBIOLOGY, (2003 Feb) 11 (2) 56-9.
Journal code: 9310916. ISSN: 0966-842X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20030225
Last Updated on STN: 20030528
Entered Medline: 20030527
AB Efficient budding of HIV from the plasma membrane requires a small peptide motif, Pro-Thr/Ser-Ala-Pro (PTAP), located near the amino terminus of the p6 **Gag** protein. Studies from several laboratories have demonstrated that the ability of p6 to stimulate HIV budding requires a direct interaction between the PTAP motif and the host endosomal sorting protein **TSG101**. The structure of the PTAP-**TSG101** binding site has recently been solved, providing valuable insights into this crucial protein-protein interaction.

L1 ANSWER 5 OF 13 MEDLINE
AN 2002642937 MEDLINE

DN 22289677 PubMed ID: 12379843
TI Structure of the **Tsg101** UEV domain in complex with the PTAP motif of the HIV-1 p6 protein.
AU Pornillos Owen; Alam Steven L; Davis Darrell R; Sundquist Wesley I
CS Department of Biochemistry, University of Utah, Salt Lake City, Utah 84132, USA.
SO NATURE STRUCTURAL BIOLOGY, (2002 Nov) 9 (11) 812-7.
Journal code: 9421566. ISSN: 1072-8368.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1M4P; PDB-1MAQ
EM 200211
ED Entered STN: 20021029
Last Updated on STN: 20021211
Entered Medline: 20021125
AB The structural proteins of HIV and Ebola display PTAP peptide motifs (termed 'late domains') that recruit the human protein **Tsg101** to facilitate virus budding. Here we present the solution structure of the UEV (ubiquitin E2 variant) binding domain of **Tsg101** in complex with a PTAP peptide that spans the late domain of HIV-1 p6(**Gag**). The UEV domain of **Tsg101** resembles E2 ubiquitin-conjugating enzymes, and the PTAP peptide binds in a bifurcated groove above the vestigial enzyme active site. Each PTAP residue makes important contacts, and the Ala 9-Pro 10 dipeptide binds in a deep pocket of the UEV domain that resembles the X-Pro binding pockets of SH3 and WW domains. The structure reveals the molecular basis of HIV PTAP late domain function and represents an attractive starting point for the design of novel inhibitors of virus budding.

L1 ANSWER 6 OF 13 MEDLINE
AN 2002630643 MEDLINE
DN 22276321 PubMed ID: 12388682
TI **Tsg101**, an inactive homologue of ubiquitin ligase e2, interacts specifically with human immunodeficiency virus type 2 **gag** polyprotein and results in increased levels of ubiquitinated **gag**
.
AU Myers Erin L; Allen Jane F
CS Department of Medicine, Addenbrooke's Hospital, Cambridge CB2 2QQ, United Kingdom.
SO JOURNAL OF VIROLOGY, (2002 Nov) 76 (22) 11226-35.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 20021022
Last Updated on STN: 20021217
Entered Medline: 20021203
AB The final stages of budding and release of a retroviral particle from the cell require the late (L) domain of **Gag**. Recently, ubiquitin and ubiquitin ligases have been implicated in the late stages of retroviral budding. In a yeast two-hybrid screen of a T-cell cDNA library to identify cellular proteins that interact with human immunodeficiency virus type 2 (HIV-2) **Gag** polyprotein, we identified **Tsg101**, an inactive homologue of ubiquitin ligase E2. **Tsg101** and HIV-2 **Gag** interact specifically in vitro and in vivo. The interaction requires the L domain PTAPP motif in the p6 domain of HIV-2 **Gag** and the N-terminal Ubc-conjugation homology domain of **Tsg101**. **Tsg101** is incorporated into HIV-2 virions. Expression of the N-terminal Ubc-conjugation homology domain of **Tsg101** inhibits the release of HIV-2 virus particles.

Overexpression of **Tsg101** results in an increase in the level of ubiquitination of HIV-2 **Gag**. Our results provide evidence for recruitment of the ubiquitination machinery of the cell during late stages of the viral life cycle, mediated by the viral **Gag** protein.

L1 ANSWER 7 OF 13 MEDLINE
AN 2002328109 MEDLINE
DN 22001147 PubMed ID: 12006492
TI Structure and functional interactions of the **Tsg101** UEV domain.
AU Pornillos Owen; Alam Steven L; Rich Rebecca L; Myszka David G; Davis Darrell R; Sundquist Wesley I
CS Department of Biochemistry and Center for Biomolecular Interactions Analysis, University of Utah, Salt Lake City 84132, USA.
SO EMBO JOURNAL, (2002 May 15) 21 (10) 2397-406.
Journal code: 8208664. ISSN: 0261-4189.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020620
Last Updated on STN: 20020713
Entered Medline: 20020712
AB Human **Tsg101** plays key roles in HIV budding and in cellular vacuolar protein sorting (VPS). In performing these functions, **Tsg101** binds both ubiquitin (Ub) and the PTAP tetrapeptide 'late domain' motif located within the viral **Gag** protein. These interactions are mediated by the N-terminal domain of **Tsg101**, which belongs to the catalytically inactive ubiquitin E2 variant (UEV) family. We now report the structure of **Tsg101** UEV and chemical shift mapping of the Ub and PTAP binding sites. **Tsg101** UEV resembles canonical E2 ubiquitin conjugating enzymes, but has an additional N-terminal helix, an extended beta-hairpin that links strands 1 and 2, and lacks the two C-terminal helices normally found in E2 enzymes. PTAP-containing peptides bind in a hydrophobic cleft exposed by the absence of the C-terminal helices, whereas ubiquitin binds in a novel site surrounding the beta-hairpin. These studies provide a structural framework for understanding how **Tsg101** mediates the protein-protein interactions required for HIV budding and VPS.

L1 ANSWER 8 OF 13 MEDLINE
AN 2002235960 MEDLINE
DN 21970296 PubMed ID: 11973141
TI **Tsg101**: HIV-1's ticket to ride.
AU Carter Carol A
CS Department of Molecular Genetics & Microbiology, Life Sciences Bldg, SUNY at Stony Brook, Stony Brook, NY 11794-5222, USA.. ccarter@ms.cc.sunysb.edu
SO TRENDS IN MICROBIOLOGY, (2002 May) 10 (5) 203-5.
Journal code: 9310916. ISSN: 0966-842X.
CY England: United Kingdom
DT News Announcement
LA English
FS Priority Journals
EM 200208
ED Entered STN: 20020426
Last Updated on STN: 20030228
Entered Medline: 20020801
AB Recent studies implicate the vacuolar protein-sorting pathway in the transport of the retroviral structural precursor (**Gag**) protein to its budding site on the plasma membrane of infected cells. This exploitation of the cellular endocytic trafficking machinery to release viral particles could lead to the identification of virus-specific modulators and provide opportunities to design new targeted anti-viral agents.

L1 ANSWER 9 OF 13 MEDLINE
AN 2002229952 MEDLINE
DN 21964413 PubMed ID: 11967285
TI Viral late domains.
AU Freed Eric O
CS Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-0460, USA.. EFreed@nih.gov
SO JOURNAL OF VIROLOGY, (2002 May) 76 (10) 4679-87. Ref: 87
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020423
Last Updated on STN: 20020611
Entered Medline: 20020607

L1 ANSWER 10 OF 13 MEDLINE
AN 2002079067 MEDLINE
DN 21664427 PubMed ID: 11805336
TI Overexpression of the N-terminal domain of **TSG101** inhibits HIV-1 budding by blocking late domain function.
AU Demirov Dimiter G; Ono Akira; Orenstein Jan M; Freed Eric O
CS Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-0460, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2002 Jan 22) 99 (2) 955-60.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020128
Last Updated on STN: 20020430
Entered Medline: 20020429
AB Efficient budding of HIV-1 from the plasma membrane of infected cells requires the function of a 6-kDa protein known as p6. A highly conserved Pro-Thr-Ala-Pro (PTAP) motif (the "late" or "L" domain), is critical for the virus-budding activity of p6. Recently, it was demonstrated that the product of tumor susceptibility gene 101 (**TSG101**), which contains at its N terminus a domain highly related to ubiquitin-conjugating (E2) enzymes, binds HIV-1 **Gag** in a p6-dependent fashion. We examined the impact of overexpressing the N-terminal region of **TSG101** on HIV-1 particle assembly and release. We observed that this domain (referred to as TSG-5') potently inhibits virus production. Examination of cells coexpressing HIV-1 **Gag** and TSG-5' by electron microscopy reveals a defect in virus budding reminiscent of that observed with p6 L domain mutants. In addition, the effect of TSG-5' depends on an intact p6 L domain; the assembly and release of virus-like particles produced by **Gag** mutants lacking a functional p6 PTAP motif is not significantly affected by TSG-5'. Furthermore, assembly and release of murine leukemia virus and Mason-Pfizer monkey virus are insensitive to TSG-5'. TSG-5' is incorporated into virions, confirming the **Gag/TSG101** interaction in virus-producing cells. Mutations that inactivate the p6 L domain block TSG-5' incorporation. These data demonstrate a link between the E2-like domain of **TSG101** and HIV-1 L domain function, and

indicate that **TSG101** derivatives can act as potent and specific inhibitors of HIV-1 replication by blocking virus budding.

L1 ANSWER 11 OF 13 MEDLINE
AN 2001680658 MEDLINE
DN 21583803 PubMed ID: 11726971
TI HIV-1 and Ebola virus encode small peptide motifs that recruit **Tsg101** to sites of particle assembly to facilitate egress.
CM Comment in: Nat Med. 2001 Dec;7(12):1278-80
AU Martin-Serrano J; Zang T; Bieniasz P D
CS Aaron Diamond AIDS Research Center and The Rockefeller University, New York, New York, USA.
NC AI50111 (NIAID)
SO NATURE MEDICINE, (2001 Dec) 7 (12) 1313-9.
Journal code: 9502015. ISSN: 1078-8956.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200201
ED Entered STN: 20011203
Last Updated on STN: 20020125
Entered Medline: 20020110
AB Retroviral **Gag** proteins encode sequences, termed late domains, which facilitate the final stages of particle budding from the plasma membrane. We report here that interactions between **Tsg101**, a factor involved in endosomal protein sorting, and short peptide motifs in the HIV-1 **Gag** late domain and Ebola virus matrix (EbVp40) proteins are essential for efficient egress of HIV-1 virions and Ebola virus-like particles. EbVp40 recruits **Tsg101** to sites of particle assembly and a short, EbVp40-derived **Tsg101**-binding peptide sequence can functionally substitute for the HIV-1 **Gag** late domain. Notably, recruitment of **Tsg101** to assembling virions restores budding competence to a late-domain-defective HIV-1 in the complete absence of viral late domain. These studies define an essential virus-host interaction that is conserved in two unrelated viruses. Because the **Tsg101** is recruited by small, conserved viral sequence motifs, agents that mimic these structures are potential inhibitors of the replication of these lethal human pathogens.

L1 ANSWER 12 OF 13 MEDLINE
AN 2001548315 MEDLINE
DN 21479121 PubMed ID: 11595185
TI **Tsg101** and the vacuolar protein sorting pathway are essential for HIV-1 budding.
AU Garrus J E; von Schwedler U K; Pornillos O W; Morham S G; Zavitz K H; Wang H E; Wettstein D A; Stray K M; Cote M; Rich R L; Myszka D G; Sundquist W I
CS Department of Biochemistry, University of Utah School of Medicine, Salt Lake City, UT 84132, USA.
NC P32 GM07464 (NIGMS)
SO CELL, (2001 Oct 5) 107 (1) 55-65.
Journal code: 0413066. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011015
Last Updated on STN: 20030228
Entered Medline: 20011204
AB Like other enveloped viruses, HIV-1 uses cellular machinery to bud from infected cells. We now show that **Tsg101** protein, which functions in vacuolar protein sorting (Vps), is required for HIV-1 budding. The UEV domain of **Tsg101** binds to an essential

tetrapeptide (PTAP) motif within the p6 domain of the structural **Gag** protein and also to ubiquitin. Depletion of cellular **Tsg101** by small interfering RNA arrests HIV-1 budding at a late stage, and budding is rescued by reintroduction of **Tsg101**. Dominant negative mutant Vps4 proteins that inhibit vacuolar protein sorting also arrest HIV-1 and MLV budding. These observations suggest that retroviruses bud by appropriating cellular machinery normally used in the Vps pathway to form multivesicular bodies.

L1 ANSWER 13 OF 13 MEDLINE
AN 2001385009 MEDLINE
DN 21332273 PubMed ID: 11427703
TI **Tsg101**, a homologue of ubiquitin-conjugating (E2) enzymes, binds the L domain in HIV type 1 Pr55(**Gag**).
AU VerPlank L; Bouamr F; LaGrassa T J; Agresta B; Kikonyogo A; Leis J; Carter C A
CS Department of Molecular Genetics and Microbiology, State University of New York, Stony Brook, NY 11794-5222, USA.
NC CA38046 (NCI)
CA52047 (NCI)
GM 48294 (NIGMS)
GM 58271 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Jul 3) 98 (14) 7724-9.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200108
ED Entered STN: 20010813
Last Updated on STN: 20030105
Entered Medline: 20010809
AB Ubiquitination appears to be involved in virus particle release from infected cells. Free ubiquitin (Ub), as well as Ub covalently bound to a small fraction of p6 **Gag**, is detected in mature HIV particles. Here we report that the p6 region in the Pr55(**Gag**) structural precursor polyprotein binds to **Tsg101**, a putative Ub regulator that is involved in trafficking of plasma membrane-associated proteins. **Tsg101** was found to interact with **Gag** in (i) a yeast two-hybrid assay, (ii) in vitro coimmunoprecipitation by using purified Pr55(**Gag**) and rabbit reticulocyte lysate-synthesized **Tsg101**, and (iii) in vivo in the cytoplasm of COS cells transfected with **gag**. The PTAPP motif [or late (L) domain] within p6, which is required for release of mature virus from the plasma membrane, was the determinant for binding Pr55(**Gag**). The N-terminal region in **Tsg101**, which is homologous to the Ubc4 class of Ub-conjugating (E2) enzymes, was the determinant of interaction with p6. Mutation of Tyr-110 in **Tsg101**, present in place of the active-site Cys that binds Ub in E2 enzymes, and other residues unique to **Tsg101**, impaired p6 interaction, indicating that features that distinguish **Tsg101** from active E2 enzymes were important for binding the viral protein. The results link L-domain function in HIV to the Ub machinery and a specific component of the cellular trafficking apparatus.

```
=> s gag and tumor
        10319 GAG
         1334 GAGS
        10868 GAG
                (GAG OR GAGS)
       509858 TUMOR
       225318 TUMORS
```

```
        612669 TUMOR
                  (TUMOR OR TUMORS)
L2         957 GAG AND TUMOR

=> s l2 and comples
             59 COMPLES
              9 COMPLESES
             68 COMPLES
                  (COMPLES OR COMPLESES)
L3            0 L2 AND COMPLES

=> s l2 and complex
         386566 COMPLEX
         112689 COMPLEXES
         452276 COMPLEX
                  (COMPLEX OR COMPLEXES)
L4           91 L2 AND COMPLEX

=> s l4 and interaction
         224938 INTERACTION
         206120 INTERACTIONS
         389101 INTERACTION
                  (INTERACTION OR INTERACTIONS)
L5           20 L4 AND INTERACTION

=> rem dup l1,l5
DUP IS NOT VALID HERE
The DELETE command is used to remove various items stored by the
system.

To delete a saved query, saved answer set, saved L-number list, SDI
request, batch request, mailing list, or user-defined cluster, format,
or search field, enter the name.  The name may include ?  for left,
right, or simultaneous left and right truncation.

Examples:

  DELETE BIO?/Q           - delete query names starting with BIO
  DELETE ?DRUG/A          - delete answer set names ending with DRUG
  DELETE ?ELEC?/L         - delete L-number lists containing ELEC
  DELETE ANTICOAG/S       - delete SDI request
  DELETE ENZYME/B         - delete batch request
  DELETE .MYCLUSTER       - delete user-defined cluster
  DELETE .MYFORMAT        - delete user-defined display format
  DELETE .MYFIELD         - delete user-defined search field
  DELETE NAMELIST MYLIST - delete mailing list

To delete an ordered document or an offline print, enter its
number.

Examples:

  DELETE P123001C         - delete print request
  DELETE D134002C         - delete document order request

To delete an individual L-number or range of L-numbers, enter the
L-number or L-number range.  You may also enter DELETE LAST followed
by a number, n, to delete the last n L-numbers.  RENUMBER or
NORENUMBER may also be explicitly specified to override the value of
SET RENUMBER.

Examples:

  DELETE L21              - delete a single L-number
```

```
  DELETE L3-L6           - delete a range of L-numbers
  DELETE LAST 4          - delete the last 4 L-numbers
  DELETE L33-            - delete L33 and any higher L-number
  DELETE -L55            - delete L55 and any lower L-number
  DELETE L2-L6 RENUMBER - delete a range of L-numbers and
                          renumber remaining L-numbers
  DELETE RENUMBER        - renumber L-numbers after deletion of
                          intermediate L-numbers

Entire sets of saved items, SDI requests, batch requests, user-defined
items, or E-numbers can be deleted.

Examples:

  DELETE SAVED/Q - delete all saved queries
  DELETE SAVED/A - delete all saved answer sets
  DELETE SAVED/L - delete all saved L-number lists
  DELETE SAVED   - delete all saved queries, answer sets,
                   and L-number lists
  DELETE SAVED/S - delete all SDI requests
  DELETE SAVED/B - delete all batch requests
  DELETE CLUSTER - delete all user-defined clusters
  DELETE FORMAT  - delete all user-defined display formats
  DELETE FIELD   - delete all user-defined search fields
  DELETE SELECT  - delete all E-numbers
  DELETE HISTORY - delete all L-numbers and restart the
                   session at L1

To delete an entire multifile SDI request, enter DELETE and
the name of the request.  To delete a component from the
multifile SDI, enter DELETE and the name of the component.

=> s l5 not l1
L6          20 L5 NOT L1

=> sdisplay l5
SDISPLAY IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> display l5
ENTER ANSWER NUMBER OR RANGE (1):1-20
ENTER DISPLAY FORMAT (BIB):bib abs

L5   ANSWER 1 OF 20     MEDLINE
AN   2003111902     MEDLINE
DN   22497601   PubMed ID: 12610113
TI   Retroviruses have differing requirements for proteasome function in the
     budding process.
AU   Ott David E; Coren Lori V; Sowder Raymond C 2nd; Adams Julian; Schubert
     Ulrich
CS   AIDS Vaccine Program, SAIC-Frederick, Inc., National Cancer Institute at
     Frederick, Frederick, Maryland 21702-1201, USA.. ott@ncifcrf.gov
NC   NO1-CO-12400 (NCI)
SO   JOURNAL OF VIROLOGY, (2003 Mar) 77 (6) 3384-93.
     Journal code: 0113724. ISSN: 0022-538X.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200304
ED   Entered STN: 20030311
     Last Updated on STN: 20030403
```

Entered Medline: 20030402

AB Proteasome inhibitors reduce the budding of human immunodeficiency virus types 1 (HIV-1) and 2, simian immunodeficiency virus, and Rous sarcoma virus. To investigate this effect further, we examined the budding of other retroviruses from proteasome inhibitor-treated cells. The viruses tested differed in their **Gag** organization, late (L) domain usage, or assembly site from those previously examined. We found that proteasome inhibition decreased the budding of murine leukemia virus (plasma membrane assembly, PPPY L domain) and Mason-Pfizer monkey virus (cytoplasmic assembly, PPPY L domain), similar to the reduction observed for HIV-1. Thus, proteasome inhibitors can affect the budding of a virus that assembles within the cytoplasm. However, the budding of mouse mammary **tumor** virus (MMTV; cytoplasmic assembly, unknown L domain) was unaffected by proteasome inhibitors, similar to the proteasome-independent budding previously observed for equine infectious anemia virus (plasma membrane assembly, YPDL L domain). Examination of MMTV particles detected **Gag**-ubiquitin conjugates, demonstrating that an **interaction** with the ubiquitination system occurs during assembly, as previously found for other retroviruses. For all of the cell lines tested, the inhibitor treatment effectively inactivated proteasomes, as measured by the accumulation of polyubiquitinated proteins. The ubiquitination system was also inhibited, as evidenced by the loss of monoubiquitinated histones from treated cells. These results and those from other viruses show that proteasome inhibitors reduce the budding of viruses that utilize either a PPPY- or PTAP-based L domain and that this effect does not depend on the assembly site or the presence of monoubiquitinated **Gag** in the virion.

L5 ANSWER 2 OF 20 MEDLINE
AN 2002680963 MEDLINE
DN 22329055 PubMed ID: 12441668
TI Glycosaminoglycan-lipoprotein **interaction**.
AU Olsson U; Ostergren-Lunden G; Moses J
CS Wallenberg Laboratory for Cardiovascular Research, Goteborg University, Sahlgrenska University Hospital, Goteborg, Sweden..
urban.olsson@eu.amershambiosciences.com
SO GLYCOCONJUGATE JOURNAL, (2001 Oct) 18 (10) 789-97.
Journal code: 8603310. ISSN: 0282-0080.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20021121
Last Updated on STN: 20030226
Entered Medline: 20030225

AB Glycosaminoglycans (**GAGs**) bound to various proteoglycans (PGs) present in the cardiovascular system have been proposed to perform a wide range of functions. These include conferring viscoelastic properties; interacting with and modulating growth factors and enzymes; and as receptors and co-receptors in lipoprotein metabolism. Binding of apoB-100 lipoproteins, particularly low density lipoproteins (LDL), to **GAGs** of extracellular matrix PGs in arteries has been proposed to be an initiating event in development of atherosclerosis. This study was initiated with the aim of getting an overview of the binding patterns of different lipoprotein subclasses with individual **GAG** categories. We thus evaluated the **interaction** of lipoproteins with **GAGs** commonly found in the cardiovascular system using a gel mobility-shift assay developed for this purpose. The same procedure was used to measure lipoproteins binding to metabolically [(35)S]-labeled whole PGs prepared from three cell types, arterial smooth muscle cells, THP-1 macrophages and from HepG2 cells. The effect of **GAG** composition on PGs on lipoprotein binding was evaluated by enzymatic degradation of the carbohydrate chains. Heparan sulfate was found to bind

beta very low density lipoproteins (beta-VLDL) and a chylomicron remnant model (beta-VLDL+apoE), but not LDL. Dermatan sulfate was found to bind LDL, but not beta-VLDL or the chylomicron remnant model. Chondroitin sulfate and heparin were found to bind all lipoproteins tested (LDL, beta-VLDL and beta-VLDL+apoE) although with different affinities. We can conclude that each lipoprotein subclass tested binds a specific assortment of the **GAGs** tested. The observations made contribute to the understanding of new and **complex** mechanisms by which carbohydrate and lipid metabolism may be linked.

L5 ANSWER 3 OF 20 MEDLINE
AN 2001684489 MEDLINE
DN 21587440 PubMed ID: 11730344
TI A new analytical scale DNA affinity binding assay for analyses of specific protein-DNA **interactions**.
AU Kumar N V; Bernstein L R
CS Department of Pathology and Laboratory Medicine, Texas A & M University System Health Science Center, College Station, TX 77843, USA.
NC R29 CA 73783 (NCI)
SO ANALYTICAL BIOCHEMISTRY, (2001 Dec 15) 299 (2) 203-10.
Journal code: 0370535. ISSN: 0003-2697.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20011204
Last Updated on STN: 20020403
Entered Medline: 20020327
AB We describe a rapid analytical assay for identification of proteins binding to specific DNA sequences. The DAPSTER assay (DNA affinity preincubation specificity test of recognition assay) is a DNA affinity chromatography-based microassay that can discriminate between specific and nonspecific protein-DNA **interactions**. The assay is sensitive and can detect protein-DNA **interactions** and larger multicomponent **complexes** that can be missed by other analytical methods. Here we describe in detail the optimization and utilization of the DAPSTER assay to isolate AP-1 **complexes** and associated proteins in multimeric **complexes** bound to the AP-1 DNA element. (c)2001 Elsevier Science.

L5 ANSWER 4 OF 20 MEDLINE
AN 2000499378 MEDLINE
DN 20431782 PubMed ID: 10974201
TI Inhibition of HIV-1 protease by a boron-modified polypeptide.
AU Pivazyan A D; Matteson D S; Fabry-Asztalos L; Singh R P; Lin P F; Blair W; Guo K; Robinson B; Prusoff W H
CS Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510, USA.. pivazya@attglobal.net
SO BIOCHEMICAL PHARMACOLOGY, (2000 Oct 1) 60 (7) 927-36.
Journal code: 0101032. ISSN: 0006-2952.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 200010
ED Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001019
AB Six boronated tetrapeptides with the carboxy moiety of phenylalanine replaced by dihydroxyboron were synthesized, and their activities against human immunodeficiency virus 1 (HIV-1) protease subsequently investigated. The sequences of these peptides were derived from HIV-1 protease substrates, which included the C-terminal part of the scissile bond

(Phe-Pro) within the **gag**-pol polyprotein. Enzymatic studies showed that these compounds were competitive inhibitors of HIV-1 protease with K(i) values ranging from 5 to 18 microM when experiments were performed at high enzyme concentrations (above 5 x 10(-8) M); however, at low protease concentrations inhibition was due in part to an increase of the association constants of the protease subunits. Ac-Thr-Leu-Asn-PheB inhibited HIV-1 protease with a K(i) of 5 microM, whereas the non-boronated parental compound was inactive at concentrations up to 400 microM, which indicates the significance of boronation in enzyme inhibition. The boronated tetrapeptides were inhibitory to an HIV-1 protease variant that is resistant to several HIV-1 protease inhibitors. Finally, fluorescence analysis showed that the **interactions** between the boronated peptide Ac-Thr-Leu-Asn-PheB and HIV-1 protease resulted in a rapid decrease of fluorescence emission at 360 nm, which suggests the formation of a compound/enzyme **complex**. Boronated peptides may provide useful reagents for studying protease biochemistry and yield valuable information toward the development of protease dimerization inhibitors.

L5 ANSWER 5 OF 20 MEDLINE
AN 1999395137 MEDLINE
DN 99395137 PubMed ID: 10464301
TI The p185(neu)-containing glycoprotein **complex** of a microfilament-associated signal transduction particle. Purification, reconstitution, and molecular associations with p58(**gag**) and actin.
AU Li Y; Hua F; Carraway K L; Carraway C A
CS Department of Biochemistry and Molecular Biology, University of Miami School of Medicine, Miami, Florida 33101, USA.
NC CA72577 (NCI)
GM 33795 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Sep 3) 274 (36) 25651-8.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991014
Last Updated on STN: 20000303
Entered Medline: 19991007
AB Microfilaments associate with the microvillar membrane of 13762 ascites mammary adenocarcinoma cells via a large transmembrane **complex** (TMC) comprising the major glycoproteins TMC-gp120, -110, -80, -65, and -55, the receptor kinase p185(neu), and the cytoplasmic proteins actin and p58(**gag**), linking the receptor with microfilaments in a signal transduction particle. Immunoblot screening with polyclonal antisera to TMC glycoproteins showed selective epithelial expression in normal rat tissues and epithelially derived **tumor** cells. The TMC glycoproteins were isolated by solubilization of microfilament core preparations in SDS, dilution, and separation on a concanavalin A-agarose affinity column. The large p185(neu)-containing **complex** was reconstituted from the column eluate after displacement of SDS with nonionic detergent, demonstrated by gel filtration and co-immunoprecipitation of the glycoproteins with anti-gp55 or anti-p185(neu). Exhaustive biotinylation of the glycoproteins gave a stoichiometry of gp120:gp110:gp80:gp65:gp55 of approximately 1:1:1:0.5:1. Overlay blots with biotinylated actin and in vitro translated, [(35)S]methionine-labeled p58(**gag**), respectively, showed specific **interactions** of actin with gp55 and gp120 and of p58(**gag**) with gp65 and gp55. These results provide evidence for a specific **complex** of microfilament-associated glycoproteins containing p185(neu) and p58(**gag**) and suggest a role for the **complex** in signal transduction scaffolding.

L5 ANSWER 6 OF 20 MEDLINE
AN 1999292859 MEDLINE
DN 99292859 PubMed ID: 10364315
TI Formation of virus assembly intermediate **complexes** in the cytoplasm by wild-type and assembly-defective mutant human immunodeficiency virus type 1 and their association with membranes.
AU Lee Y M; Liu B; Yu X F
CS Department of Molecular Microbiology and Immunology, Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Maryland 21205, USA.
NC AI-35525 (NIAID)
SO JOURNAL OF VIROLOGY, (1999 Jul) 73 (7) 5654-62.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199907
ED Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990723
AB We have previously identified two distinct forms of putative viral assembly intermediate **complexes**, a detergent-resistant **complex** (DRC) and a detergent-sensitive **complex** (DSC), in human immunodeficiency virus type 1 (HIV-1)-infected CD4(+) T cells (Y. M. Lee and X. F. Yu, Virology 243:78-93, 1998). In the present study, the intracellular localization of these two viral assembly intermediate **complexes** was investigated by use of a newly developed method of subcellular fractionation. In wild-type HIV-1-infected H9 cells, the DRC fractionated with the soluble cytoplasmic fraction, whereas the DSC was associated with the membrane fraction. The DRC was also detected in the cytoplasmic fraction in H9 cells expressing HIV-1 Myr- mutant **Gag**. However, little of the unmyristylated **Gag** and **Gag**-Pol proteins was found in the membrane fraction. Furthermore, HIV-1 **Gag** proteins synthesized in vitro in a rabbit reticulocyte lysate system in the absence of exogenous lipid membrane were able to assemble into a viral **Gag complex** similar to that of the DRC identified in infected H9 cells. The density of the viral **Gag complex** was not altered by treatment with the nonionic detergent Triton X-100, suggesting a lack of association of this **complex** with endogenous lipid. Formation of the DRC was not significantly affected by mutations in assembly domains M and L of the **Gag** protein but was drastically inhibited by a mutation in the assembly I domain. Purified DRC could be disrupted by high-salt treatment, suggesting electrostatic **interactions** are important for stabilizing the DRC. The **Gag** precursor proteins in the DRC were more sensitive to trypsin digestion than those in the DSC. These findings suggest that HIV-1 **Gag** and **Gag**-Pol precursors assemble into DRC in the cytoplasm, a process which requires the protein-protein **interaction** domain (I) in NCp7; subsequently, the DRC is transported to the plasma membrane through a process mediated by the M domain of the matrix protein. It appears that during this process, a conformational change might occur in the DRC either before or after its association with the plasma membrane, and this change is followed by the detection of virus budding structure at the plasma membrane.

L5 ANSWER 7 OF 20 MEDLINE
AN 1999262227 MEDLINE
DN 99262227 PubMed ID: 10328871
TI Binding of interferon gamma by glycosaminoglycans: a strategy for localization and/or inhibition of its activity.
AU Fernandez-Botran R; Yan J; Justus D E
CS Division of Experimental Immunology and Immunopathology, Department of

Pathology and Laboratory Medicine, University of Louisville, KY 40292, USA.. rafael@louisville.edu
NC AI-34627 (NIAID)
SO CYTOKINE, (1999 May) 11 (5) 313-25.
Journal code: 9005353. ISSN: 1043-4666.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990707
AB Glycosaminoglycans (**GAGs**) are a group of negatively charged molecules present in many tissues as components of the extracellular matrix, basement and cellular membranes. This work analysed the ability of this group of substances to interact with human interferon gamma and the effect of those **interactions** on its biologic activity. A variety of **GAGs** (heparin, heparan sulfate, chondroitin sulfate and hyaluronic acid), and a related sulfated polysaccharide (dextran sulfate), were found to interact with IFN-gamma as determined by inhibition of the binding of [125I]IFN-gamma to COLO-205 cells and binding to wells coated with **GAGs**. These **interactions** were inhibited by synthetic peptides mimicking the sequences of the basic amino acid cluster located at the C-terminal end of mouse and human IFN-gamma, or by poly-L-lysine, suggesting that ionic **interactions** between the positively-charged C-terminus and negatively charged groups in **GAGs** were involved. IFN-gamma molecules bound to plate-immobilized or endothelial cell surface **GAGs** retained biological activity, since they could induce major histocompatibility **complex** (MHC) class II expression on COLO-205 cells, suggesting that cell surface **GAGs** might be able to present IFN-gamma to its receptors. These results suggest important regulatory roles for **GAGs** on the activity of IFN-gamma in vivo.

L5 ANSWER 8 OF 20 MEDLINE
AN 1998325156 MEDLINE
DN 98325156 PubMed ID: 9658084
TI Human immunodeficiency virus type 1 replication is modulated by host cyclophilin A expression levels.
AU Yin L; Braaten D; Luban J
CS Departments of Microbiology, Columbia University, College of Physicians and Surgeons, New York, New York 10032, USA.
NC AI36199 (NIAID)
SO JOURNAL OF VIROLOGY, (1998 Aug) 72 (8) 6430-6.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980805
AB Human immunodeficiency virus type 1 (HIV-1) **Gag** and the cellular protein cyclophilin A form an essential **complex** in the virion core: virions produced by proviruses encoding **Gag** mutants with decreased cyclophilin A affinity exhibit attenuated infectivity, as do virions produced in the presence of the competitive inhibitor cyclosporine. The A224E **Gag** mutant has no effect on cyclophilin A affinity but renders HIV-1 replication cyclosporine resistant in Jurkat T cells. In contrast, A224E mutant virus is dead in H9 T cells, although replication is rescued by cyclosporine or by expression in cis of a

Gag mutant that decreases cyclophilin A-affinity. The observation that disruption of the **Gag**-cyclophilin A **interaction** rescues A224E mutant replication in H9 cells prompted experiments which revealed that, relative to Jurkat cells, H9 cells express greater quantities of cyclophilin A. The resulting larger quantity of cyclophilin A shown to be packaged into virions produced by H9 cells is presumably disruptive to the A224E mutant virion core. Further evidence that increased cyclophilin A expression in H9 cells is of functional relevance was provided by the finding that **Gag** mutants with decreased cyclophilin A affinity are dead in Jurkat cells but capable of replication in H9 cells. Similarly, cyclosporine concentrations which inhibit wild-type HIV-1 replication in Jurkat cells stimulate HIV-1 replication in H9 cells. These results suggest that HIV-1 virion infectivity imposes narrow constraints upon cyclophilin A stoichiometry in virions and that infectivity is finely tuned by host cyclophilin A expression levels.

L5 ANSWER 9 OF 20 MEDLINE
AN 1998206724 MEDLINE
DN 98206724 PubMed ID: 9546647
TI Inter-alpha-trypsin inhibitor proteoglycan family--a group of proteins binding and stabilizing the extracellular matrix.
AU Bost F; Diarra-Mehrpour M; Martin J P
CS INSERM U.295, Faculte de Medecine Pharmacie de Rouen, St Etienne du Rouvray, France.. fbost@skcc.org
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1998 Mar 15) 252 (3) 339-46. Ref: 76
Journal code: 0107600. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980513
AB Extracellular matrix (ECM) is composed of several macromolecules associated in a **complex** network. This structure allows cells to adhere, migrate and interact. Hyaluronic acid (HA) is a glycosaminoglycan (**GAG**) and a major representative of ECM. HA-binding proteins such as CD44, aggrecan, and versican, have been implicated in structuring the ECM by stabilizing large macromolecular aggregates. They also play an important role in **tumor** metastasis and cell motility. Recently, further HA-binding proteins were identified: the inter-alpha-trypsin inhibitor(ITI)-related proteins. ITI is a glycoprotein composed of three polypeptides: two heavy chains (HC1 and HC2) and one light chain (bikunin). Bikunin confers the protease-inhibitor function. The heavy chains' function was unknown. Recent studies have shown that HC1 and HC2 are linked in vivo and in vitro to hyaluronic acid. This linkage greatly improves extracellular matrix stability. It also demonstrates that ITI-related proteins might be considered as HA-binding proteins (HABP). The ITI related proteins are composed of four polypeptides (HC1, HC2, HC3 and the bikunin) encoded by four genes H1, H2, H3 and L. Unlike the majority of plasma protein a non-disulfide covalent linkage exists between heavy chains and bikunin. This review presents the recent progress concerning the **interactions** between ITI and ECM showing that ITI-related proteins are HABP members. We will focus on the heavy chain linkage with HA, which represents the demonstration of covalent binding between proteins and HA.

L5 ANSWER 10 OF 20 MEDLINE
AN 1998153684 MEDLINE
DN 98153684 PubMed ID: 9485332
TI Comparison of the DNA binding characteristics of the related zinc finger

proteins WT1 and EGR1.
AU Hamilton T B; Borel F; Romaniuk P J
CS Department of Biochemistry and Microbiology, University of Victoria, British Columbia, Canada.
SO BIOCHEMISTRY, (1998 Feb 17) 37 (7) 2051-8.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
ED Entered STN: 19980326
Last Updated on STN: 20000303
Entered Medline: 19980317
AB The **interactions** of the related zinc finger proteins WT1 and EGR1 with DNA have been investigated using a quantitative binding assay. A recombinant peptide containing the four zinc fingers of WT1 binds to the dodecamer DNA sequence GCG-TGG-GCG-TGT with an apparent dissociation constant (Kd) of (1.14 +/- 0.09) x 10(-9) M under conditions of 0.1 M KCl, pH 7.5, at 22 degrees C. Under the same conditions, a recombinant peptide containing the three zinc fingers of EGR1 binds to the dodecamer sequence, the first nine bases comprising the EGR consensus binding site, with an apparent Kd of (3.55 +/- 0.24) x 10(-9) M. The nature of the equilibrium binding of each peptide to DNA was investigated as a function of temperature, pH, monovalent salt concentration, and divalent salt concentration. The **interaction** of WT1 with DNA is an entropy-driven process, while the formation of the EGR1-DNA **complex** is favored by enthalpy and entropy. The DNA binding activities of both proteins have broad pH optima centered at pH 8.0. The binding of both proteins to DNA shows similar sensitivity to ionic strength, with approximately 7.7 +/- 0.8 ion pairs formed in the EGR1-DNA **complex** and 9.2 +/- 1.8 ion pairs formed in the WT1-DNA **complex**. Results of measuring the effects of point mutations in the DNA binding site on the affinity of WT1 and EGR1 indicates a significant difference in the optimal binding sites: for EGR1, the highest affinity binding site has the sequence GNG-(T/G)GG-G(T/C)G, while for WT1 the highest affinity binding site has the sequence G(T/C)G-(T/G)GG-**GAG**-(T/C)G(T/C).

L5 ANSWER 11 OF 20 MEDLINE
AN 1998058977 MEDLINE
DN 98058977 PubMed ID: 9395524
TI Platelet factor 4 binds to glycanated forms of thrombomodulin and to protein C. A potential mechanism for enhancing generation of activated protein C.
AU Dudek A Z; Pennell C A; Decker T D; Young T A; Key N S; Slungaard A
CS Department of Internal Medicine, University of Minnesota, Minneapolis, Minnesota 55455, USA.
NC CA59510 (NCI)
R29-HL55219 (NHLBI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Dec 12) 272 (50) 31785-92.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980129
Last Updated on STN: 20021210
Entered Medline: 19980115
AB Platelet factor 4 (PF4) is an abundant platelet alpha-granule heparin-binding protein. We have previously shown that PF4 accelerates up to 25-fold the proteolytic conversion of protein C to activated protein C by the thrombin.thrombomodulin **complex** by increasing its

affinity for protein C 30-fold. This stimulatory effect requires presence of the gamma-carboxyglutamic acid (Gla) domain in protein C and is enhanced by the presence of a chondroitin sulfate glycosaminoglycan (**GAG**) domain on thrombomodulin. We hypothesized that cationic PF4 binds to both protein C and thrombomodulin through these anionic domains. Qualitative SDS-polyacrylamide gel electrophoresis analysis of avidin extracts of solutions containing biotinylated PF4 and candidate ligands shows that PF4 binds to **GAG**+ but not **GAG**- forms of thrombomodulin and native but not Gla-domainless protein C. Quantitative analysis using the surface plasmon resonance-based BIAcoreTM biosensor system confirms the extremely high affinity of PF4 for heparin (KD = 4 nM) and shows that PF4 binds to **GAG**+ thrombomodulin with a KD of 31 nM and to protein C with a KD of 0.37 microM. In contrast, PF4 had no measurable **interaction** with **GAG**- thrombomodulin or Gla-domainless protein C. Western blot analysis of normal human plasma extracted with biotinylated PF4 demonstrates PF4 binding to protein C in a physiologic context. Thus, PF4 binds with relative specificity and high affinity to the **GAG**- domain of thrombomodulin and the Gla domain of protein C. These **interactions** may enhance the affinity of the thrombin.thrombomodulin **complex** for protein C and thereby promote the generation of activated protein C.

L5 ANSWER 12 OF 20 MEDLINE
AN 97445166 MEDLINE
DN 97445166 PubMed ID: 9300051
TI Ribonuclease and high salt sensitivity of the ribonucleoprotein **complex** formed by the human LINE-1 retrotransposon.
AU Hohjoh H; Singer M F
CS Laboratory of Biochemistry, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SO JOURNAL OF MOLECULAR BIOLOGY, (1997 Aug 8) 271 (1) 7-12.
Journal code: 2985088R. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971021
Last Updated on STN: 19990129
Entered Medline: 19971008
AB P40 is encoded by the first open reading frame of the human LINE-1 retrotransposon and is found in a large cytoplasmic ribonucleoprotein (RNP) **complex**, the p40 RNP-**complex**, in association with LINE-1 RNA(s) in human teratocarcinoma cell lines. We report here investigations on the stability of the p40 RNP-**complex** against various nucleases and high salt (0.5 M NaCl) treatment. The results indicate that (1) the p40 RNP-**complex** is dissociated after ribonuclease or high salt treatment, (2) DNase I does not disrupt the **complex**, (3) after dissociation of the **complex**, p40 maintain protein-protein **interactions** but in smaller **complexes**, and (4) p40 is not associated with the LINE-1 RNA(s) after high salt treatment. These observations suggest that the RNA molecule(s) is(are) essential for the stability of the large p40 **complex** and that the **complex** has a structure which allows various nucleases to reach the RNA. These features are distinct from those of typical virus and virus-like particles of retroviruses and other retrotransposons, respectively. Together with the fact that no significant sequence homology exists between p40 and the **gag** and **gag**-like proteins, it is likely that the p40 RNP-**complex** is structurally different from the typical virus and virus-like particles.

L5 ANSWER 13 OF 20 MEDLINE
AN 96400134 MEDLINE
DN 96400134 PubMed ID: 8806510

TI Inhibition of HIV-1 replication by cyclosporine A or related compounds correlates with the ability to disrupt the **Gag**-cyclophilin A **interaction**.
AU Franke E K; Luban J
CS Department of Medicine, Columbia University, College of Physicians and Surgeons, New York, New York 10032, USA.
NC AI64199 (NIAID)
SO VIROLOGY, (1996 Aug 1) 222 (1) 279-82.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199610
ED Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961031
AB The HIV-1 **Gag** polyprotein specifically incorporates the cellular peptidylprolyl isomerase cyclophilin A into virions. HIV-1 replication is inhibited by cyclosporine A, an immunosuppressive drug which binds with high affinity to cyclophilin A and precludes **interaction** with the **Gag** polyprotein. Using a panel of four drugs, including cyclosporine A, two nonimmunosuppressive analogues of cyclosporine A which bind to cyclophilin A but which cannot form a tertiary **complex** with the calcium-dependent phosphatase calcineurin, and the structurally unrelated immunosuppressant FK506, we demonstrated that the antiviral effect of cyclosporine A is not due to blockade of calcineurin-mediated signal transduction pathways. Rather, the effectiveness of cyclosporine A and related compounds at inhibiting HIV-1 replication correlates with cyclophilin A-binding affinity and with the ability to disrupt the **interaction** between cyclophilin A and the HIV-1 **Gag** polyprotein. These results support the contention that the **Gag** -cyclophilin A **interaction** is required for HIV-1 replication.

L5 ANSWER 14 OF 20 MEDLINE
AN 96351076 MEDLINE
DN 96351076 PubMed ID: 8752279
TI Positional cloning of the mouse retrovirus restriction gene Fv1.
CM Comment in: Nature. 1996 Aug 29;382(6594):762-3
AU Best S; Le Tissier P; Towers G; Stoye J P
CS Division of Virology, National Institute for Medical Research, London, UK.
SO NATURE, (1996 Aug 29) 382 (6594) 826-9.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
OS GENBANK-X97719; GENBANK-X97720
EM 199703
ED Entered STN: 19970407
Last Updated on STN: 19980206
Entered Medline: 19970321
AB Vertebrate evolution has taken place against a background of constant retrovirus infection, and much of the mammalian genome consists of endogenous retrovirus-like elements. Several host genes have evolved to control retrovirus replication, including Friend-virus-susceptibility-1, Fv1, on mouse chromosome 4 (refs 3, 4). The Fv1 gene acts on murine leukaemia virus at a stage after entry into the target cell but before integration and formation of the provirus. Although restriction is not absolute, Fv1 prevents or delays spontaneous or experimentally induced viral tumours. In vitro, Fv1 restriction leads to an apparent 50-1,000 fold reduction in viral titre. Genetic evidence implicates a direct **interaction** between the Fv1 gene product and a component of the viral preintegration **complex**, the capsid protein CA (refs 7-9).

We have now cloned Fv1: the gene appears to be derived from the **gag** region of an endogenous retrovirus unrelated to murine leukaemia virus, implying that the Fv1 protein and its target may share functional similarities despite the absence of nucleotide-sequence homology.

L5 ANSWER 15 OF 20 MEDLINE
AN 96288442 MEDLINE
DN 96288442 PubMed ID: 8679287
TI Aspects of molecular **interaction** between HIV p17 and human gamma interferon.
AU Flamminio G; Caruso A; Poiesi C; Bonfanti C; Terlenghi L; Donato Canaris A; Varinacci C; Martinelli F; Garotta G; Albertini A; +
CS Institute of Microbiology, University of Brescia, Italy.
SO AIDS RESEARCH AND HUMAN RETROVIRUSES, (1995 Dec) 11 (12) 1441-7.
Journal code: 8709376. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199608
ED Entered STN: 19960828
Last Updated on STN: 19990129
Entered Medline: 19960816
AB We describe the specific **interaction** between high-purity recombinant human immunodeficiency virus (HIV) type 1 p17 and human gamma interferon (hIFN-gamma) proteins. This **interaction** was found to be dose dependent and to involve conformational epitopes on both sides. Specificity was confirmed by competition ELISA, using monoclonal antibodies (MAbs) to hIFN-gamma as specific reagents. By competition experiments we also identified the epitope(s) on the hIFN-gamma molecule involved in p17 binding, very close to the receptor binding site. The kinetic constants were determined by surface plasmon resonance (SPR) analysis. The affinity constant (KA) of the **complex** was 2.78 x 10(8) M-1, that is, the ratio between a low dissociation rate constant (Koff)(1 x 10(-5)sec-1) and a high association rate constant (Kon) (3 x 10(3) M-1sec-1). However, p17 did not displace the binding of hIFN-gamma to its cellular receptor, nor did it interfere with the capability of the lymphokine to induce de novo expression of HLA-DR antigens on human monocytic cells or to inhibit the proliferation of **tumor** cells.

L5 ANSWER 16 OF 20 MEDLINE
AN 96240644 MEDLINE
DN 96240644 PubMed ID: 8659115
TI Evidence for direct association of Vpr and matrix protein p17 within the HIV-1 virion.
AU Sato A; Yoshimoto J; Isaka Y; Miki S; Suyama A; Adachi A; Hayami M; Fujiwara T; Yoshie O
CS Shionogi Institute for Medical Science, Osaka, Japan.
SO VIROLOGY, (1996 Jun 1) 220 (1) 208-12.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199608
ED Entered STN: 19960808
Last Updated on STN: 19990129
Entered Medline: 19960801
AB Vpr is one of the auxiliary proteins of HIV-1 and is selectively incorporated into the virion by a process involving the C-terminal p6 portion of the **Gag** precursor Pr55. Vpr and the matrix protein p17 are the components of the viral preintegration **complex** and appear to play important roles in the nuclear transport of proviral DNA in

nondividing cells. In the present study, we have demonstrated by coimmunoprecipitation experiments that Vpr associates with matrix protein p17 but not with capsid protein p24 within the HIV-1 virion. Experiments employing the yeast two-hybrid GAL4 assay for protein-protein **interactions** also demonstrated a direct association between Vpr and the C-terminal region of matrix protein p17. Association of Vpr and the matrix protein p17 within the mature virion is consistent with their collaborative role in the nuclear transportation of the viral preintegration **complex** in nondividing cells such as macrophages.

L5 ANSWER 17 OF 20 MEDLINE
AN 94253065 MEDLINE
DN 94253065 PubMed ID: 8195143
TI Molecular cloning and sequencing of a 58-kDa membrane- and microfilament-associated protein from ascites **tumor** cell microvilli with sequence similarities to retroviral **Gag** proteins.
AU Juang S H; Huang J; Li Y; Salas P J; Fregien N; Carraway C A; Carraway K L
CS Department of Biochemistry and Molecular Biology, University of Miami School of Medicine, Florida 33101.
NC CA 14395 (NCI)
GM 33795 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 May 27) 269 (21) 15067-75.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
OS GENBANK-U15425
EM 199406
ED Entered STN: 19940707
Last Updated on STN: 19970203
Entered Medline: 19940629
AB The MAT-C1 subline of the 13762 rat mammary adenocarcinoma has highly stable, branched microvilli and immobile cell surface receptors. A membrane- and microfilament-associated 58-kDa protein (p58) in the MAT-C1 microvilli has been implicated in the stabilization of the microvilli and microfilament-membrane **interactions**. This protein is associated with a high M(r) glycoprotein **complex** containing the (proto)oncogene p185neu and other signal transduction components in a putative microfilament-associated signal transduction particle. Amino acid sequences were obtained from two trypsin peptides of p58. Screening a MAT-C1 cDNA library with a degenerate oligonucleotide derived from the larger peptide and polymerase chain reaction amplification of cDNA ends permitted the isolation of overlapping cDNAs encoding the 427-amino acid open reading frame of p58. In vitro transcription and translation using a full-length cDNA gave a protein of approximately 55 kDa, which reacts with anti-p58 antiserum and reconstitutes into a **complex** with actin and glycoproteins from the membrane-microfilament **interaction** site. When COS-7 cells were transfected with the full-length cDNA, p58 was localized in a punctate distribution. In addition, the transfected cells exhibited fewer microfilament cables than untransfected neighboring cells. The amino acid sequence showed a surprising similarity to mammalian retroviral **Gag** proteins and included regions corresponding to p15, p12 and the N-terminal 80% of p30. Comparisons of p58 and the corresponding regions of the **Gag** proteins for Moloney murine leukemia virus indicated that about 60% of their amino acid residues were identical. These studies suggest that p58 is the product of an endogenous retroviral gene whose expression as a cellular protein alters the properties of the **tumor** cell to provide a selective advantage for **tumor** growth in the animal.

L5 ANSWER 18 OF 20 MEDLINE
AN 93078750 MEDLINE

DN 93078750 PubMed ID: 1448082
TI A common intermediary factor (p52/54) recognizing "acidic blob"-type domains is required for transcriptional activation by the Jun proteins.
CM Erratum in: Mol Cell Biol 1993 Mar;13(3):1981
AU Oehler T; Angel P
CS Kernforschungszentrum Karlsruhe, Institut fur Genetik und Toxikologie, Germany.
SO MOLECULAR AND CELLULAR BIOLOGY, (1992 Dec) 12 (12) 5508-15.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199212
ED Entered STN: 19930129
Last Updated on STN: 19970203
Entered Medline: 19921229
AB The ability of the c-Jun protein, the main component of the transcription factor AP1, to interact directly or indirectly with the RNA polymerase II-initiation **complex** to activate transcription was investigated by in vivo transcription interference ("squelching") experiments. Coexpression of a Jun mutant lacking its DNA binding domain strongly represses the activity of wild-type c-Jun. Repression depends on the presence of the transactivation domains (TADs), suggesting that a limiting factor interacting with the TADs is essential to link Jun and the components of the transcriptional machinery. The activity of this intermediary factor(s) is restricted to TADs characterized by an abundance of negatively charged amino acids, as demonstrated by the abilities of the TADs of JunB, GAL4, and VP16 to repress c-Jun activity. Depending on the presence of the TADs of Jun, we found physical **interaction** between Jun and a cluster of three proteins with molecular masses of 52, 53, and 54 kDa (p52/54). Association between Jun and p52/54 is strongly reduced in the presence of VP16, suggesting that the two proteins compete for binding to p52/54. Transcription factors containing a different type of TAD (e.g., GHF1, estrogen receptor, or serum response factor) fail to inhibit Jun activity, suggesting that these proteins act through a different mechanism. We consider the requirement of Jun to interact with p52/54 utilized by other transcription factors a new mechanism in the regulation of transcription of Jun-dependent target genes.

L5 ANSWER 19 OF 20 MEDLINE
AN 90185188 MEDLINE
DN 90185188 PubMed ID: 2516828
TI Different requirements for formation of Jun: Jun and Jun: Fos **complexes**.
AU Smeal T; Angel P; Meek J; Karin M
CS Department of Biology, School of Medicine, University of California at San Diego, La Jolla 92093.
SO GENES AND DEVELOPMENT, (1989 Dec) 3 (12B) 2091-100.
Journal code: 8711660. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199004
ED Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900426
AB The cFos proto-oncoprotein associates with cJun to form a heterodimer with increased DNA binding and transcriptional activities. It has been suggested that dimerization of these proteins is mediated by the interdigitation of an orderly repeat of leucine residues forming a leucine zipper. In agreement with this model, we find that binding to the AP-1 site requires dimerization of these proteins. Although cFos, itself, does

not seem to dimerize and bind to the AP-1 site, Jun: Fos heterodimers have higher stability than Jun homodimers, which accounts for their increased DNA binding activity. Mutational analysis indicates that at least three of the repeated leucines of cJun are important for homodimer formation. However, these residues can be mutated without affecting formation of Jun: Fos heterodimers. In addition, several other residues present between the leucines are also important for both homo- and heterodimerization. These findings provide support for the recent proposal that these proteins dimerize via formation of a coiled coil and suggest that residues other than leucines provide specificity for this **interaction**.
Assuming that dimerization is required for proper alignment of the DNA recognition sites, we generated a cJun mutant containing a small insertion between the dimerization and the DNA recognition domains. This mutant fails to bind DNA, but it acts as a trans-dominant inhibitor of cJun and cFos because it still dimerizes with the wild-type proteins.

L5 ANSWER 20 OF 20 MEDLINE
AN 81028310 MEDLINE
DN 81028310 PubMed ID: 6252348
TI Murine mammary **tumor** virus structural protein **interactions**: formation of oligomeric **complexes** with cleavable cross-linking agents.
AU Racevskis J; Sarkar N H
NC CA-08748 (NCI)
CA-16599 (NCI)
CA-17129 (NCI)
SO JOURNAL OF VIROLOGY, (1980 Sep) 35 (3) 937-48.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198012
ED Entered STN: 19900316
Last Updated on STN: 19970203
Entered Medline: 19801216
AB Murine mammary **tumor** virus protein **interactions** in the intact virion structure were studied with the use of the cleavable cross-linking reagents dithiobis(succinimidyl propionate) and methyl 4-mercaptobutyrimidate hydrochloride. Cross-linked oligomeric **complexes** of murine mammary **tumor** virus proteins were analyzed by two-dimensional gel electrophoresis. Among the **complexes** most consistently formed were a heterodimer of the two glycoproteins gp36 and gp52, the homodimer of gp36, and the homotrimer of gp52. A very prominent oligomer formed at higher concentrations of dithiobis(succinimidyl propionate) was a **complex** of about 230,000 molecular weight, made up of three molecules each of gp36 and gp52. A number of lines of evidence, including electron microscopic analysis, suggest that the 230,000-molecular-weight **complex** actually represents the murine mammary **tumor** virus spike structure. Of the murine mammary **tumor** virus core proteins, p14 forms homooligomers most readily. Upon cross-linking with methyl 4-mercaptobutyrimidate hydrochloride a small amount of what seems to be a heterodimer made up of the N-terminal **gag** protein p10 and the hydrophobic membrane glycoprotein gp36 can be observed.